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being unemployed did not influence patients' perceived stress levels during the COVID-19 pandemic.

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#### **MATURE HUMAN OOCYTES AND PRE-IMPLANTATION EMBRYOS ARE SUSCEPTIBLE TO SARS-COV-2 INFECTION BASED ON THE PRESENCE OF ACE2 AND TMPRSS2 PROTEINS.**



Sandeep K. Rajput, PhD,<sup>1</sup> Deirdre Logsdon, MS,<sup>1</sup> Shaihl A. Khan, PhD,<sup>2</sup> Rebecca Kile, MS,<sup>1</sup> Heidi J. Engelhorn, MS,<sup>3</sup> Ye Yuan, PhD,<sup>1</sup> Sue McCormick, BS,<sup>1</sup> William B. Schoolcraft, MD,<sup>3</sup> Rebecca L. Krisher, PhD,<sup>3</sup> <sup>1</sup>Colorado Center for Reproductive Medicine, Lone Tree, CO; <sup>2</sup>Post-Doctoral Research Associate, Lone Tree, CO; <sup>3</sup>CCRM Colorado, Lone Tree, CO.

**OBJECTIVE:** SARS-CoV-2 entry in host cells requires the presence of angiotensin-converting enzyme 2 (ACE2) as the extracellular receptor, and the serine protease TMPRSS2 to cleave the viral spike protein for incorporation into the host cell. Basigin (BSG/CD147) may also act as an ACE2 independent receptor mechanism. The cysteine protease cathepsin-L (CTSL) may also cleave the viral spike proteins and facilitate cell entry. The objective of this study was to characterize the mRNA and protein expression of these cellular entry receptors and proteases in female reproductive cells to determine their susceptibility to SARS-CoV-2 infection.

**DESIGN:** Prospective Research Study.

**MATERIALS AND METHODS:** Materials and Methods: Oocytes (GV, MII), follicular cells (cumulus, CC; granulosa, GC) and embryos (1 cell, 1C; blastocyst, BL) were collected from a minimum of three different patients per sample type, with consent. Samples were analyzed for mRNA expression of *ACE2*, *CD147*, *TMPPSS2*, and *CTSL* genes relative to GAPDH using RT-qPCR. Primers were validated using human mixed tissue cDNA. Protein quantification was performed by immunoblotting using the Jess system (ProteinSimple) optimized to detect over 10 proteins/5-10 oocytes or embryos. Antibodies for ACE2, CD147, TMPPSS2, and CTSL proteins were validated and then used to determine protein abundance relative to total protein. Data were obtained from three independent biological replicates and analyzed using one-way ANOVA.

**RESULTS:** Results from q-PCR analysis revealed high ( $p < 0.05$ ) abundance of *ACE2* transcripts in GV and MII oocytes compared to CC, GC, and BL. *ACE2* protein was present in all the samples, but was relatively higher ( $p < 0.17$ ) in M2 oocytes, 1C, BL, and CC compared to GV oocytes and GC. *TMPPSS2* protein was abundant in MII oocytes, 1C, and BL, and was present but at low levels in GV oocytes and follicular cells. Protein abundance of CD147 was five-fold higher ( $p < 0.05$ ) in GV and ~1.5 fold higher in GC compared to all other samples analyzed. No CTSL protein was observed with the expected molecular weight (38 kD), although a 55 kD band (a possible isoform) was detected in GV oocytes and CC.

**CONCLUSIONS:** Cumulus and granulosa cells are least susceptible to SARS-CoV-2 infection due to the lack of required receptors and proteases. Co-expression of the protein for ACE2 and TMPPSS2 in MII oocytes, zygotes, and blastocysts suggests that these reproductive cells are susceptible to SARS-CoV-2 infection. In conclusion, using a combined approach of mRNA and protein analysis from the same samples suggests that mature human oocytes and preimplantation embryos have the cellular machinery required for SARS-Cov2 entry, although we do not know if this occurs in vivo. The potential for viral infection in oocytes and embryos has important ramifications for ART. Care must be taken to avoid introduction of the virus to the embryo while in the ART laboratory, as well as potentially introducing the virus from an infected embryo to laboratory workspaces.

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#### **WE ARE HERE FOR YOU: INFERTILITY CLINIC WEBSITE COMMUNICATION DURING THE ESCALATING STAGES OF THE COVID-19 PANDEMIC.**



Holly Mehr, MD MSED,<sup>1</sup> Tia Jackson-Bey, MD MPH,<sup>2</sup> Michelle Vu, MD,<sup>2</sup> Victoria Lee, BS,<sup>1</sup> Christopher Herndon,

MD,<sup>3</sup> Jacqueline Ho, MD MS,<sup>4</sup> Lusine Aghajanova, MD PhD,<sup>5</sup> Molly M. Quinn, MD,<sup>1</sup> <sup>1</sup>University of California, Los Angeles, Los Angeles, CA; <sup>2</sup>University of Illinois at Chicago, College of Medicine, Chicago, IL; <sup>3</sup>University of Washington, Seattle, WA; <sup>4</sup>University of Southern California, Los Angeles, CA; <sup>5</sup>Stanford University, Stanford, CA.

**OBJECTIVE:** On March 17th, ASRM published guidance for REI clinics regarding infertility treatment during the COVID-19 pandemic. The recommendations advised against initiation of new fertility treatment cycles outside of emergent fertility preservation. Our objective was to evaluate what SART-member fertility clinics communicated to the public and their patients via clinic websites during this time period.

**DESIGN:** Cross-sectional study.

**MATERIALS AND METHODS:** Between 4/20/20 and 4/24/20, SART-member fertility clinic websites were reviewed for REI-specific COVID-19 messages (REI-CM). The REI-CM was evaluated for: type of treatment offered, and to whom; adherence to updated ASRM guidance; and citation of ASRM (or other) guidance. Each website was evaluated by two reviewers and arbitrated by a third in the case of discrepancies. Practice size, type, and location were abstracted from SART. Clinics were classified by whether they were under a shelter in place (SIP) order and the duration of that order. Chi squared analyses were performed to determine associations between clinic demographics and patterns in messaging.

**RESULTS:** 381 SART-member clinics maintained active websites. Of those, 249 (65.3%) had REI-CM. The presence of REI-CM was more common in private than academic practices (73% vs 38%,  $p < 0.001$ ) and with increasing practice volume: 38% of clinics with <200 annual cycles vs 91% of clinics with >1000 cycles ( $p < 0.001$ ). There was a trend toward increased REI-CM use in states with a SIP order for  $\geq 30$  days (70% of 212,  $p = 0.064$ ).

ASRM guidance was cited in 61% ( $n = 152$ ) of REI-CM; however, only 33% ( $n = 82$ ) outlined treatment practices that reflected ASRM guidance published at the time of the data extraction. Adherence to ASRM guidelines was more common in academic than private practices (54% vs 31%,  $p = 0.02$ ) but was not correlated with size of practice or geographic region.

Conversely, 18% ( $n = 44$ ) of practices announced treating patients on a "case-by-case basis" with definitions ranging from specific ("women with AMH <0.7") to vague ("as determined by our providers alongside our patients"). Additionally, 9% of REI-CM ( $n = 23$ ) announced continued treatment regardless of a patient's clinical urgency. This messaging was more common in groups doing >1000 cycles a year (18%,  $p = 0.009$ ), with a trend toward practices in the northeast (16%,  $p = 0.113$ ) and in states with SIP orders lasting <30 days (14%,  $p = 0.09$ ). Clinics treating all-comers were less likely to cite ASRM than other clinics (41% vs 62%,  $p = 0.045$ ). However, 75% ( $n = 14$ ) cited COVID-19 guidance from WHO, CDC and state and local governments.

**CONCLUSIONS:** While public messaging may not reflect the actual practices of a clinic, this study reveals heterogeneity in how clinics incorporated ASRM recommendations and responded to the early stages of the COVID-19 pandemic. Academic practices were more likely to indicate their adherence to ASRM recommendations. High volume groups were more likely to communicate with their patients about what treatments they offered and to treat patients outside ASRM guidance. Lessons learned may inform optimal response in future waves of COVID-19.

References: American Society for Reproductive Medicine. Patient Management and Clinical Recommendations During The Coronavirus (COVID-19) Pandemic. Available at <https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate2.pdf>. Accessed on May 26, 2020

**P-171** 4:30 PM Saturday, October 17, 2020

#### **THE IMPACT OF CORONAVIRUS DISEASE 2019 (COVID-19) ON THE RELATIONSHIP BETWEEN THE STRESS LEVELS OF IN VITRO FERTILIZATION (IVF) PATIENTS AND THE AMOUNT OF TIME SPENT TRYING TO GET PREGNANT.**



Ariana Kam, BA,<sup>1</sup> Jennifer Gottfried, BS,<sup>2</sup> Julia E. Miesleszko, BA,<sup>2</sup> You J. Kim, BS,<sup>2</sup> Mehriiso Khaydarova, BS,<sup>2</sup> Edward J. Nejat, MD, FACOG,<sup>2</sup> Janelle Luk, MD, FACOG,<sup>2</sup> <sup>1</sup>Generation Next Fertility, New York, NY; <sup>2</sup>■■■■■.

**OBJECTIVE:** The objective of this study was to determine the impact of coronavirus disease 2019 (COVID-19) on in vitro fertilization (IVF) patients' stress levels, insomnia, and risk of post-traumatic stress disorder (PTSD) relative to the amount of time each patient spent trying to get pregnant.